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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,995	01/17/2001	Yuhpyng L. Chen	PC10759A	5772

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 04/01/2004

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,995	CHEN, YUHPYNG L.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *13,16*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Applicant's amendment of 07-17-03 has been fully considered. Although the amended claim 1 has overcome the previous rejection of 112/2nd paragraph, it raises new ground(s) of rejection.

Applicant's terminal disclaimer of 07-17-03 has overcome the previous double patenting rejection, and thus, said rejection is withdrawn herein.

Claims 1-22 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-7, and 9-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 recites the definition of R_{24} and R_{25}, which includes the broad limitation of "*C_1-C_4 haloalkyl*", followed by narrow limitations of "***especially*** *CF_3, CHF_2, CF_2CF_3, or CH_2CF_3*".

b. Claims 9 and 10 recite the broad limitation of "*pain perception*" followed by the narrow limitation of "*such as fibromyalgia*". They also recite the broad limitation of "*mood disorders*" followed by narrow limitations of "*depression,*

including major depression, single episode depression, recurrent depression, child abuse induced depression". Likewise, they recite the broad limiation of "*inflammatory disorders*" followed by narrow limitations of "*such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies*".

c. Claims 14 and 20 recite the broad limitation of "*selective serotonin reuptake inhibitors*" followed by narrow limitations of "*sertraline, fluoxetine*". They also recite the broad limitation of "*tricyclic antidepressants*" followed by narrow limitations of "*imipramine, amitriptyline, trimipramine, doxepin, desipramine, nortiptyline, protriptyline,..., clomipramine*"

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

d. Claims 2-7, and 11-22 are rejected as being dependent on claim 1, and carry over limitations of the compounds in claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being **enabling** for the treatment of *abnormal circadian rhythm, depression, and emesis*, does **not** reasonably provide **enable**ment for the treatment of other diseases such as rheumatoid arthritis, osteoarthritis, asthma, psoriasis, allergies, mood disorders (various depression disorders), ulcer, bipolar, phobias, addictions, ischemic neuronal damage, epilepsy, stroke, immune dysfuction, urinary incontinence, Parkinson's disease, Hungtington's disease, Alzheimer's type, hypertension, tachycardia, osteoporosis, premature birth, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claim 9 recites a pharmaceutical composition to treat a myriad of diseases ranging from arthritis, to bovine shipping fever to premature birth. Claim 10 recites a method of treating all those diseases listed in claim 9. The disorders recited in both claims do not share the same etiology, nor do they affect from the same organ or tissue.

For example, "inflammatory disorders" cover an array of diseases such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies, which have different symptoms on various tissues (e.g, bone and muscle for arthritis; nerve for pain; lung for asthma; skin for psoriasis; eyes, ears, nose and sinuses for allergies).

Likewise, mood disorders, Alzheimer's disease, Parkinson's disease, Huntington's disease, bipolar, epilepsy—all affect the body in different ways although they are related neurological system. That is, Parkinson's disease is related to dopamine receptors while Alzheimer's disease is associated with the unavailability of acetylcholine. Similarly, epilepsy is known to be related to

GABA receptors while Huntington's disease has no known cause, and bipolar is treated with lithium carbonate.

Similarly, other diseases covered by those claims (such as phobias, ischemic neuronal damage, immune dysfunction, urinary incontinence, hypertension, tachycardia, osteoporosis, premature birth,...etc.) all have different causative factors, which affect distinct biological pathways.

The amount of direction or guidance presented: The specification only provides references to determine CRF antagonist activity of the active compounds. However, there is no data for the claimed compounds as CRF antagonists. Thus, given the myriad of compounds and various treatments claimed herein, the cited references do not serve as adequate enblement.

The state of the prior art: Currently, the drugs that treat arthritis (in general) do not treat asthma, psoriasis, or allergies. Even anti-asthmatic drugs can not treat psoriasis or allergies. Similarly, the commercially available antihistamines cannot treat arthritis (of any kind), nor can it treat asthma or psoriasis. Likewise, none of the commercially available antidepressants, or antipsychotic agents cant treat arthritis, asthma, Parkinson's diseases, Alzheimer's diseases, urinary incontinence, immune dysfunction, osteoporosis, ulcer, or premature birth. Thus, the composition and method of treating a plethora of diseases using one set of compounds are contrary to the practice of medicine as a whole.

Thus, given the broad scope of the claims, limited teaching, and the **unpredictable nature** of the pharmaceutical art, the **skilled clinician** would have to carry out **undue experimentation** to a pharmaceutical composition that can treat the many diseases claimed herein.

3. **Enablement:** Claims 12-16, and 18-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 12-16 are drawn to a treatment that requires a second therapeutic agents. Claims 18-22 are drawn to a pharmaceutical composition having the claimed compound, and a second therapeutic agent. However, many of the second therapeutic agents can have adverse drug interactions. For example, carbamazepine interferes with the metabolism of other drugs, and thus, can reduce the bioavailability of other drugs. Therefore , without a guidance on how these agents can be combined, one skilled in the art would have to carry out undue experimentation to combine the claimed compounds and other therapeutic agents to treat abnormal circadian rhythm, depression and emesis.

Double Patenting

4. The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d

1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 9, and 10 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 13, 14, 29-35, and 37-40 of copending Application No. 09/ 580,791. Although the conflicting claims are not identical, they are not patentably distinct from each other because the formula (I) in the copending application 09/ 580,791 encompass the formula (I) claimed herein, especially when A is CR_7.

Formula (I) of 09/ 580,791 differs from the instant formula (I) by having R_1 and R_2 representing "*C_1-C_6 hydrocarbyl*" and "*C_1-C_{12} hydrocarbyl*" (respectively) which is broader than the scope of the instant R_1 and R_2. However, such a difference would still render obvious the instant formula (I) because one skilled in the art would have understood that hydrocarbyl group includes alkyl, alkenyl, alkynyl, cycloalkyl, and aryl group. The same composition and methods of treatment are claimed in both instances.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1, 3, 5-11, and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by **Chen** (WO 95/33750). On pages 55, and 59, Examples 84 and 98 disclose compounds that are embraced by the instant formula (I) in claim 1 with the following substituents:

A is CR_7 wherein R_7 is hydrogen;

R_3 is methyl;

B is $-NR_1R_2$ wherein R_1 and R_2 are independently an C_2-C_3 alkyl group;

R_4 is either $-C(O)NR_{24}R_{25}$ or $-COOR_{24}$ wherein R_{24} is either hydrogen or alkyl, and R_{25} is hydrogen;

Z is –O-; R_5 is aryl (or phenyl).

Said compounds read on the instant claim 3 with R_4 as $-C(O)NR_{24}R_{25}$. They read on the instant claim 5 with R_4 as $-COOCH_3$. They read on claims 6 and 7 with Z as O, and B as $-NHCHR_1R_2$ wherein R_1 and R_2 are both alkyl groups. The disclosed compounds are also CRF antagonists and can treat diseases as listed in claims 9-11, and 17 (see pages 7

and 8 of WO'750). On page 6, Chen lists a species on line 8 that reads on the last species in the instant claim 8. Therefore, Chen's teaching also anticipates the instant claim 8.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-T (~10 am ~ 8:30 pm) starting from February 22nd, 2004.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at 571-272-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting SPE of 1624, at 571-272-0661.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

T. Truong
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March 23, 2004

MUKUND J. SHAH
SUPERVISORY PATENT EXAMINER
GROUP 1600